Remarks

Claims 34, 39-44, 46-50, and 52-55 are pending. Claims 1-33, 35-38, 45, and 51 have been canceled.

Rejection Under 35 U.S.C. § 102

1. Claims 34, 39-44, 47-48, and 52-55 were rejected under 35 U.S.C. § 102(e), as being anticipated by Lupski et al. (5,691,136). Applicants respectfully traverse this rejection.

Lupski et al. discloses oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting (See Lupski et al. column 1, lines 10-20). The method described by Lupski et al. employs primers that are used to amplify bacterial genomic DNA between repetitive sequences present in the bacterial genomes. (Id.) Each primer pair disclosed within Lupski et al. is selected to be complementary to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17).

In making a rejection under 35 U.S.C. § 102, the Patent Office is burdened with establishing that the cited art teaches each and every limitation of the claims. Applicants submit that the present rejection does not meet this burden.

The passages of Lupski et al. cited in the Office Action fail to disclose a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising, in part, a set of primers wherein the set of primers comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence, and wherein the random portion is complementary to the target sequence. The passages of Lupski et al. cited in the Office Action also fail to disclose a kit for amplifying a target nucleic acid sequence, the kit comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, and wherein the set of primers has 3 or more primers.

Claims 34, 39-44, 52 and 54

Claim 34, as well as claims 39-44, 52 and 54 that depend from Claim 34, are drawn to a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising a set of primers wherein the set of primers comprises primers having random nucleotide sequences, and a strand displacing DNA polymerase or a DNA polymerase and strand displacement factor compatible with the DNA polymerase, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) a set of primers, wherein the set of primers comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion, (see claim 34, lines 3-6) wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence (see claim 47, lines 6-8) and (2) wherein the random portion is complementary to the target sequence.

The Office Action admits (page 3, lines 1-2) that Lupski et al does not explicitly disclose that each primer has a constant portion and a random portion; however the Office Action alleges that Lupski et al. inherently teaches that each primer has a constant portion and a random portion and the constant portion of each primer are the same. The Office Action bases this on Figures 2 and 3 of Lupski et al. Specifically, the Office Action alleges that the primers have a constant portion, TT, GGG, and AA (citing Figure 3) and a random portion comprises ATCG , citing Figure 2). First, Applicants note that the Office Action is citing separate primer pairs for separate target sequences. Figure 3 of Lupski et al. depicts primers directed to the ERIC consensus whereas Figure 2 depicts primers directed to the REP consensus. Thus, Applicants submit that the alleged evidence of primers with constant and random portions is misguided. Specifically, the Office Action has failed to cite relevant portions of Lupski et al. that depict where "each primer" has a constant and a random portion. The Office Action has alleged that the primers directed to the REP consensus have random portions and that the primers directed to the ERIC

consensus have constant portions, but has failed to cite where the primers directed to the REP consensus have constant portions or where the primers directed to the ERIC consensus have random portions. In short, the Office Action has failed to show where Lupski et al. teaches that each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. Furthermore, Applicants submit that such a showing is not possible as Lupski et al. fails to contain such a teaching. As such, Applicants respectfully submit that the Office Action has failed to meet its' burden of establishing that the cited art teaches each and every limitation of the claims.

In addition to the Office Action's failure to direct the Applicants to where Lupski et al. teaches all of the claimed elements, Applicants further submit that even taking all of the disclosures of Lupski et al. together, Lupski et al fails to teach all the elements of the claimed invention. For example, even if Applicants were to follow the Office Action's allegation that the primers of Figures 2 and 3 should be viewed as one, to wit Applicants respectfully disagree, the constant portions, as alleged by the Office Action, would not be the same for each primer. In other words, Lupski et al. fails to teach "wherein the constant portion of each primer has the same nucleotide sequence". If the Office Action intends on using the primers of Figures 2 and 3, the recitation by the Office Action that the constant portions are TT, GGG, and AA and that the primers of Figures 2 and 3 constitute the "primers of the set" as currently claimed, the constant portions are not present in the primers of Figure 2. As such, Applicants respectfully submit that Lupski et al. fails to teach wherein the constant portion of each primer in the primer set has the same nucleotide sequence. As such, Applicants respectfully submit that Lupski et al. fails to teach each and every limitation of the claims and therefore does not anticipate the claims.

In the interest if being fully responsive to the Office Action's remarks, Applicants take this opportunity to respond to the Office Action's retort against Applicant's previous Response. Returning to the Office Action's allegation that the primers in Figure 2 depict primers with random portions, Applicants previously noted the presence of "N' residues that represent to presence of Inosine residues within the REP consensus primers. However, as discussed in the previous Response to Office Acton, this is not a random portion complementary to the target as

claimed, nor does the Office Action appear to cite the "N" residues as such. The "N" position is simply a "wobble" base in the primer to be inserted for the purpose of maintaining uniform lengths of the primers being used in the Lupski et al. methods and not to be complementary to the target. Even if the "N" of the primers of Lupski et al. were designed to be complementary to the target, they would not be random as defined in the instant specification.

In response to applicant's argument that if the "N" primers of Lupski et al. were designed to be complementary to the target, they would not be random as defined by the instant specification, the Office Action argues that, "there is no definition regarding the phrase 'random portion'." (p. 4, lines 5-7). Applicants respectfully traverse. The specification on page 12, lines 18-25, which states:

> In a nucleic acid sample of significant complexity... specific nucleic acid sequences present in the sample need not be known and the primers need not be designed to be complementary to any particular sequence. Rather, the complexity of the nucleic acid sample results in a large number of different hybridization target sequences in the sample which will be complementary to various primers of random or partially random sequence.

Therefore, "random portion" is clearly defined in the instant specification as a portion of a primer "which is not designed to be complementary to any particular sequence," but because of the complexity of the sample, will be complementary to the target." This is significantly different than the degenerate positions in the primers of Lupski et al., which are not designed to be complementary to the target. In fact, regarding the sequences of Figure 2, Lupski et al. state that, "Degenerate 38-mer REPALL...probes were designed which encompassed the entire consensus REP sequence...Total degeneracy is represented either by any one of the four common bases (A, G, C, or T) placed at specific positions..." (Example 3, Col. 12, lines 19-32). One of skill in the art would have known that degenerate sequences are not, by definition, designed to be complementary to the target. Instead, they represent a position at which the properly complementary sequence is not known.

As discussed above, in making a rejection under 35 U.S.C. § 102, the Patent Office is burdened with establishing that the cited art teaches each and every limitation of the claims. That is clearly not the case here, as Lupski et al. does not teach or suggest that the primers disclosed

therein comprise a random portion which is complementary to the target, as specified in the instant claims.

As such, the cited passage of Lupski et al. fails to disclose a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising, in part, a set of primers wherein the set of primers comprises primers having random nucleotide sequences, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence wherein each primer comprises a constant portion and a random portion, and wherein the random portion is complementary to the target sequence. Because Lupski et al. fails to disclose every feature of the claimed kits, Lupski et al. fails to anticipate the claims. Because Lupski et al. fails to disclose every element of the claims, Applicants respectfully request withdrawal of the rejection.

Claims 47, 48, 53 and 55

Claim 47, as well as claims 48, 53 and 55 that depends from Claim 47, is drawn to a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) that the each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target (see claim 47, lines 2-4) and (2) that all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). It is important to note that each of the primers in the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action alleges (page 4, lines 7-18) that the teachings of Lupski et al. anticipates the limitations of the claims. For support, the Office Action cites sections of Lupski et al. that describe methods of identifying strains of bacteria by genomic fingerprinting as well as specific sections directed to primers that can be used in the disclosed method. Specifically, the Office Action alleges that Lupski et al. discloses that a variety of primers can be used to detect repetitive sequences in bacteria and that a plurality of primers can be added to the method where each of the primers will bind to a different sequence (see Office Action page 4, lines 9-13). It is important to note that Lupski et al. employs pairs of primers for the detection reactions. In fact, the specific portion of Lupski et al. cited by the Office Action in support of this recites:

> In addition to the above described methods a plurality of *pairs of primers* can be added to the method. Each *pair of primers* will bind to a different repetitive sequence. (*Emphasis added.*)

In other words, the only time multiple primers are disclosed to binding to different targets is in the context of primer pairs (See Lupski et al., column 8, line 65 – column 9, line 2) or where the primers of the primer pairs bind to the same portion of the same hybridization target (overlap) (See Lupski et al. Figures 2 and 3). The failure of Lupski et al. to disclose the currently claimed kits is supported in Figures 2 and 3 of Lupski et al (also cited by the Office Action), where primer pairs are described and illustrated. Each primer pair disclosed within Lupski et al. is selected to be complementary and to the same portion (overlapping) to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17). The primers described in Figure 3, as representative of the primers taught by Lupski et al. fall into two categories, those that bind the consensus/target sequence (sense) and those that bind the complement of the consensus/target sequence (antisense). Although the sense and antisense primers bind to different regions of the consensus/target sequence, they bind to different strands of the consensus/target sequence. However, each primer in the sense or antisense set, for example the ERIC1 and ERIC2 primers described above, bind to the same portion (overlap) of the consensus/target sequence on the particular strand of the target sequence. In other words, each primer in the primer set are NOT complementary to NOR do they bind to a different portion

of the hybridization target (non-overlapping). The same is true for the primers disclosed in Figure 2 for the REP sequence.

As provided above, Claim 47 is drawn to a kit that comprises, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 47, line 3-5) and wherein all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). In other words, each of the primers in the primer set each hybridize to a different portion of the hybridization target on the same strand. In the interest of being complete, Applicants note that "the same strand of the target sequence" does not include the complementary strand of the target sequence. This is supported at least on page 34, lines 25-31 of the application, where one of the amplification methods using a set of primers where all of the primers are complementary to the same strand of the target sequence is described. Specifically, it is provided that when a set of primers where all of the primers are complementary to the same strand of the target sequence are used, only one of the strands of the target sequence is replicated. This is due to the fact that the primers do not hybridize to the complementary strand. One of skill in the art would understand this to mean that the primers of the primer set only bind one of the strands, not both strands. Lupski et al. simply does not disclose such a limitation.

In response to Applicants' arguments, the Office Action alleges that, "the primers in fig.2 or fig. 3 are complementary to a different portion of a hybridization target and to the same strand of the target sequence; for example, in fig. 2, probe REPALL-I and probe REPIR-I are hybridized to the same strand of the target sequence, but the probe is complementary to a different portion of the hybridization target."(p. 4, lines 10-16). However, in making a rejection under 35 U.S.C. § 102, the Patent Office is burdened with establishing that the cited art teaches *each and every limitation of the claims*. It is noted that claim 47 includes the limitation that the set of primers include 3 or more primers wherein all of the primers in the set of primers are complementary to the same strand of the target sequence. That is clearly not the case with Lupski et al., which at best teach 2 primers that are complementary to the same strand.

In summary, Lupski et al. fails to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. Because Lupski et al. fails to disclose every feature of the claimed kits, Lupski et al. fails to anticipate claims 47-48, 53 and 55. As such, Applicants respectfully request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 103

1. Claim 49 is rejected under 35 U.S.C. § 103(a), as being unpatentable over Lupski et al. (5,691,136). Applicants respectfully traverse this rejection to the extent it applies to the claims as amended.

In order for a reference or a combination of references to anticipate a claim or claims, "[f]irst, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP § 2143.

With regard to the subject matter of Claim 49, Applicants first note that Claim 49 depends from Claim 47 and by definition encompass all the elements of Claim 47. As provided above, Claim 47 drawn to a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) that the each primer comprises a complementary portion, wherein the complementary portions of each of

the primers in the primer set are each complementary to a different portion of the hybridization target (see claim 47, lines 2-4) and (2) that all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). It is important to note that each of the primers in the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action alleges (page 4, lines 7-18) that the teachings of Lupski et al. anticipates the limitations of the claims. For support, the Office Action cites sections of Lupski et al. that describe methods of identifying strains of bacteria by genomic fingerprinting as well as specific sections directed to primers that can be used in the disclosed method. Specifically, the Office Action alleges that Lupski et al. discloses that a variety of primers can be used to detect repetitive sequences in bacteria and that a plurality of primers can be added to the method where each of the primers will bind to a different sequence (see Office Action page 4, lines 9-13). It is important to note that Lupski et al. employs pairs of primers for the detection reactions. In fact, the specific portion of Lupski et al. cited by the Office Action in support of this recites:

> In addition to the above described methods a plurality of *pairs of primers* can be added to the method. Each *pair of primers* will bind to a different repetitive sequence. (*Emphasis added.*)

In other words, the only time multiple primers are disclosed to binding to different targets is in the context of primer pairs (See Lupski et al., column 8, line 65 – column 9, line 2) or where the primers of the primer pairs bind to the same portion of the same hybridization target (overlap) (See Lupski et al. Figures 2 and 3). The failure of Lupski et al. to disclose the currently claimed kits is supported in Figures 2 and 3 of Lupski et al (also cited by the Office Action), where primer pairs are described and illustrated. Each primer pair disclosed within Lupski et al. is selected to be complementary and to the same portion (overlapping) to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17). The primers described in Figure 3, as representative of the primers taught by Lupski et al. fall into two categories, those that bind the consensus/target sequence (sense) and those that bind the complement of the consensus/target sequence (antisense). Although the sense and antisense primers bind to different regions of the consensus/target sequence, they bind to different strands

of the consensus/target sequence. However, each primer in the sense or antisense set, for example the ERIC1 and ERIC2 primers described above, bind to the same portion (overlap) of the consensus/target sequence on the particular strand of the target sequence. In other words, each primer in the primer set are NOT complementary to NOR do they bind to a different portion of the hybridization target (non-overlapping). The same is true for the primers disclosed in Figure 2 for the REP sequence.

As provided above, Claim 47 is drawn to a kit that comprises, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 47, line 3-5) and wherein all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). In other words, each of the primers in the primer set each hybridize to a different portion of the hybridization target on the same strand. In the interest of being complete, Applicants note that "the same strand of the target sequence" does not include the complementary strand of the target sequence. This is supported at least on page 34, lines 25-31 of the application, where one of the amplification methods using a set of primers where all of the primers are complementary to the same strand of the target sequence is described. Specifically, it is provided that when a set of primers where all of the primers are complementary to the same strand of the target sequence are used, only one of the strands of the target sequence is replicated. This is due to the fact that the primers do not hybridize to the complementary strand. One of skill in the art would understand this to mean that the primers of the primer set only bind one of the strands, not both strands. Lupski et al. simply does not disclose such a limitation.

Specifically, Lupski et al. fails to disclose or suggest a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or

more primers. Because Lupski et al. fails to disclose or suggest every feature of the claimed kits, Lupski et al. fails to make obvious claim 49. As such, Applicants respectfully request withdrawal of the rejection.

2. Claims 46 and 50 were rejected under 35 U.S.C. § 103(a), as being unpatentable over Lupski et al. (5,691,136) as applied to claims 32, 34-37, 39-44 and 47-49 further in view of Blanco et al. (Journal of Biological Chemistry, 1989, Vol.264(15), pg. 8935-40). Applicants respectfully traverse this rejection to the extent it applies to the claims as amended.

In order for a reference or a combination of references to anticipate a claim or claims, "[f]irst, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP § 2143.

Lupski et al. discloses oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting (See Lupiski et al. column 1, lines 10-20). The method described by Lupski et al. employs primers that are used to amplify bacterial genomic DNA between repetitive sequences present in the bacterial genomes. (Id.) Each primer pair disclosed within Lupski et al. is selected to be complementary to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17).

Claim 46 that depends from Claim 34 and Claim 50 that depends from Claim 47 all refer to the polymerase of the respective kits. Specifically, each of the claims are drawn to Φ29 DNA polymerase. Aside from the specific enumeration of a DNA polymerase, Claims 46 and 50 comprise all the limitations of the claims from which they depend.

Claim 46

With regard to the subject matter of Claim 46, Applicants first note that Claim 46 depends from Claim 34 and by definition encompass all the elements of Claim 34. As provided above, Claim 34 is drawn to a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising a set of primers

wherein the set of primers comprises primers having random nucleotide sequences, and a strand displacing DNA polymerase or a DNA polymerase and strand displacement factor compatible with the DNA polymerase, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. As such, claims 34 and 46 require the set of primers to have specific attributes and abilities. .

The Office Action relies on Lupski et al. in the same way and for the same disclosure for which Lupski et al. was applied in the 35 U.S.C. §102(e) rejection of claims 34, 39-44, 52 and 54. The Office Action further admits that Lupski et al. fails to specifically disclose a kit containing phage vphi 29 DNA polymerase for strand displacement activity (See Office Action page 8, lines 3-4).

Blanco et al. which was cited for disclosing that phage vphi 29 polymerase for strand displacement fails to supplement the elements missing from Lupski et al. As discussed above in connection with the rejection under 35 U.S.C. § 102(e), Lupski et al. fails to disclose or suggest a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising, in part, a set of primers wherein the set of primers comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion, and wherein the random portion is complementary to the target sequence.

Thus, Lupski et al. and Blanco et al., either alone or in combination, fail to disclose or suggest each and every element of claim 46. Accordingly, Lupski et al. and Blanco et al. do not make obvious claim 46. Applicants respectfully request withdrawal of this rejection.

Claim 50

With regard to the subject matter of Claim 50, Applicants first note that Claim 50 depends from Claim 47 and by definition encompass all the elements of Claim 47. As provided above, Claim 47 drawn to a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers

in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) that the each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target (see claim 47, lines 2-4) and (2) that all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). It is important to note that each of the primers in the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action relies on Lupski et al. in the same way and for the same disclosure for which Lupski et al. was applied in the 35 U.S.C. §102(e) rejection of claims 47, 48, 53 and 55. The Office Action further admits that Lupski et al. fails to specifically disclose a kit containing phage vphi 29 DNA polymerase for strand displacement activty (See Office Action page 8, lines 3-4). Blanco et al. which was cited for disclosing that phage vphi 29 polymerase for strand displacement fails to supplement the elements missing from Lupski et al.

As discussed above in connection with the rejection under 35 U.S.C. § 102(e), Lupski et al. fails to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers.

Thus, Lupski et al. and Blanco et al., either alone or in combination, fail to disclose or suggest each and every element of claim 50. Accordingly, Lupski et al. and Blanco et al. do not make obvious claim 50. Applicants respectfully request withdrawal of this rejection.

A Credit Card payment submitted via EFS Web in the amount of $245.00, representing $245.00 for the extension of time Extension of Time fee for a small entity under 37 C.F.R. § 1.17(a)(2) and a Request for Two Month Extension of Time are also enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

Scott D. Marty, Ph.D.
Registration No. 53,277

BALLARD SPAHR ANDREWS & INGERSOLL, LLP
Customer Number 23859
(678) 420-9300
(678) 420-9301 (fax)

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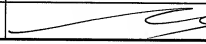
Signature		Date	1.27.09